

**Intracranial pressure responsiveness to positive end-expiratory pressure is influenced by chest wall elastance: a prospective physiological study in patients with aneurysmal subarachnoid hemorrhage**

Han Chen<sup>1,2</sup>; Kai Chen<sup>2</sup>; Jing-Qing Xu<sup>2</sup>; Ying-Rui Zhang<sup>2</sup>; Rong-Guo Yu<sup>2</sup>; Jian-Xin Zhou<sup>1\*</sup>

<sup>1</sup>: Department of Critical Care Medicine, Beijing Tiantan Hospital, Capital Medical University, Beijing, China

<sup>2</sup>: Surgical Intensive Care Unit, Fujian Provincial Clinical College, Fujian Medical University, Fuzhou, Fujian, China

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**Table E1** Respiratory mechanics at low and high positive end-expiratory pressure

|                                                   | Low positive end-expiratory pressure (5 cm H <sub>2</sub> O) |                   |                   |                             | High positive end-expiratory pressure (15 cm H <sub>2</sub> O) |                   |                   |                             | <i>p</i> value <sup>b</sup> |
|---------------------------------------------------|--------------------------------------------------------------|-------------------|-------------------|-----------------------------|----------------------------------------------------------------|-------------------|-------------------|-----------------------------|-----------------------------|
|                                                   | All patients                                                 | Responders        | Non-responders    | <i>p</i> value <sup>a</sup> | All patients                                                   | Responders        | Non-responders    | <i>p</i> value <sup>a</sup> |                             |
| V <sub>TE</sub> (mL/kg)                           | 7.7 (7.1, 8.3)                                               | 7.7 (7.2, 8.3)    | 7.7 (7.1, 8.3)    | 0.935                       | 7.7 (7.1, 8.2)                                                 | 7.7 (7.1, 8.2)    | 7.7 (7.1, 8.1)    | 0.905                       | 0.304                       |
| ΔP <sub>AW</sub> (cm H <sub>2</sub> O)            | 6.8 (6.5, 9.5)                                               | 6.8 (6.8, 9.5)    | 8.2 (5.4, 9.5)    | 0.606                       | 9.5 (7.8, 10.9)                                                | 9.5 (6.8, 10.9)   | 9.5 (8.2, 10.9)   | 0.496                       | < 0.001                     |
| ΔP <sub>CW</sub> (cm H <sub>2</sub> O)            | 2.7 (1.4, 3.1)                                               | 2.7 (2.7, 4.1)    | 1.4 (1.4, 2.7)    | 0.058                       | 2.7 (2.7, 4.1)                                                 | 4.1 (2.7, 6.8)    | 2.7 (2.7, 2.7)    | 0.019                       | 0.003                       |
| ΔP <sub>L</sub> (cm H <sub>2</sub> O)             | 4.8 (4.1, 5.8)                                               | 4.1 (2.7, 5.4)    | 5.4 (4.1, 6.8)    | 0.268                       | 6.8 (4.1, 8.2)                                                 | 5.4 (4.1, 6.8)    | 6.8 (5.4, 8.2)    | 0.330                       | 0.003                       |
| E <sub>RS</sub> (cm H <sub>2</sub> O/L)           | 15.3 (12.5, 18.6)                                            | 15.5 (12.9, 21.4) | 14.2 (11.7, 17.7) | 0.136                       | 20.1 (16.2, 23.9)                                              | 20.1 (15.7, 24.7) | 20.1 (16.3, 21.8) | 0.158                       | < 0.001                     |
| E <sub>CW</sub> (cm H <sub>2</sub> O/L)           | 5.5 (2.9, 6.9)                                               | 6.2 (5.5, 8.3)    | 3.1 (2.8, 5.4)    | 0.021                       | 6.2 (5.4, 10.2)                                                | 8.9 (6.1, 12.5)   | 5.7 (4.8, 6.3)    | 0.011                       | 0.001                       |
| E <sub>L</sub> (cm H <sub>2</sub> O/L)            | 9.4 (7.9, 12.1)                                              | 8.9 (6.2, 12.1)   | 9.5 (8.5, 11.0)   | 0.863                       | 12.9 (8.5, 15.6)                                               | 12.1 (8.2, 17.0)  | 14.7 (10.9, 15.6) | 0.970                       | 0.004                       |
| E <sub>CW</sub> /E <sub>RS</sub> ratio            | 0.33 (0.25, 0.43)                                            | 0.40 (0.29, 0.50) | 0.29 (0.25, 0.33) | 0.017                       | 0.40 (0.29, 0.47)                                              | 0.40 (0.38, 0.50) | 0.29 (0.25, 0.40) | 0.025                       | 0.247                       |
| Airway resistance<br>(cm H <sub>2</sub> O*sec /L) | 13.0 (9.9, 14.2)                                             | 12.6 (9.3, 13.5)  | 13.3 (11.8, 14.3) | 0.271                       | 12.6 (10.1, 15.0)                                              | 12.9 (10.2, 17.9) | 12.5 (9.9, 14.2)  | 0.133                       | 0.894                       |

Data are presented as median (interquartile range).

<sup>a</sup>The *p* value of inter-group comparison. <sup>b</sup>The *p* value of pre-after comparison (low positive end-expiratory pressure to high positive end-expiratory pressure) in the whole study population.

$V_{TE}$ , expiratory tidal volume;  $\Delta P_{AW}$ , airway driving pressure;  $\Delta P_{CW}$ , chest wall driving pressure;  $\Delta P_L$ , transpulmonary driving pressure;  $E_{RS}$ , respiratory system elastance;  $E_{CW}$ , chest wall elastance;  $E_L$ , lung elastance.

**Table E2** Changes in respiratory mechanics from low to high positive end-expiratory pressure level (high-low)

|                                                   | All patients       | Responders      | Non-responders     | <i>p</i> value |
|---------------------------------------------------|--------------------|-----------------|--------------------|----------------|
| $\Delta P_{AW}$ (cm H <sub>2</sub> O)             | 2.7 (1.4, 4.1)     | 2.7 (0, 4.1)    | 1.4 (1.4, 4.1)     | 0.640          |
| $\Delta P_{CW}$ (cm H <sub>2</sub> O)             | 1.4 (0, 1.4)       | 1.4 (0, 2.7)    | 1.4 (0, 1.4)       | 0.861          |
| $\Delta P_L$ (cm H <sub>2</sub> O)                | 0.7 (0, 2.7)       | 0 (0, 2.7)      | 1.4 (0, 2.7)       | 0.508          |
| $E_{RS}$ (cm H <sub>2</sub> O/L)                  | 5.3 (2.1, 8.4)     | 5.5 (0.2, 9.2)  | 3.3 (2.1, 7.6)     | 0.468          |
| $E_{CW}$ (cm H <sub>2</sub> O/L)                  | 2.7 (0, 3.1)       | 2.7 (0, 5.1)    | 2.7 (0, 3.0)       | 0.787          |
| $E_L$ (cm H <sub>2</sub> O/L)                     | 1.3 (0, 5.6)       | 0.1 (0, 6.0)    | 2.7 (0, 5.5)       | 0.520          |
| $E_{CW}/E_{RS}$ ratio                             | 0.04 (-0.06, 0.13) | 0 (-0.04, 0.11) | 0.04 (-0.08, 0.15) | 0.950          |
| Airway resistance<br>(cm H <sub>2</sub> O*sec /L) | 0.1 (-1.4, 0.9)    | 0.2 (-1.9, 3.2) | 0.1 (-1.2, 0.6)    | 0.852          |

Data are presented as median (interquartile range).

$\Delta P_{AW}$ , airway driving pressure;  $\Delta P_{CW}$ , chest wall driving pressure;  $\Delta P_L$ , transpulmonary driving pressure;  $E_{RS}$ , respiratory system elastance;  $E_{CW}$ , chest wall elastance;  $E_L$  lung elastance.

**Table E3** Intracranial pressure and hemodynamic parameters at low and high positive end-expiratory pressure

|                | Low positive end-expiratory pressure (5 cm H <sub>2</sub> O) |                    |                   |                             | High positive end-expiratory pressure (15 cm H <sub>2</sub> O) |                   |                    |                             |                             |
|----------------|--------------------------------------------------------------|--------------------|-------------------|-----------------------------|----------------------------------------------------------------|-------------------|--------------------|-----------------------------|-----------------------------|
|                | All patients                                                 | Responders         | Non-responders    | <i>p</i> value <sup>a</sup> | All patients                                                   | Responders        | Non-responders     | <i>p</i> value <sup>a</sup> | <i>p</i> value <sup>b</sup> |
| HR (beats/min) | 91.5 (70.3, 98.3)                                            | 78 (67.0, 98.0)    | 92.0 (90.0, 99.0) | 0.059                       | 90.0 (75.8, 101.5)                                             | 82.0 (68.0, 98.0) | 90.0 (80.0, 104.0) | 0.598                       | 0.857                       |
| MAP (mm Hg)    | 81.0 (75.6, 92.1)                                            | 83.7 (74.3, 101.0) | 80.1 (76.3, 84.3) | 0.559                       | 76.2 (67.4, 90.0)                                              | 82.3 (66.0, 91.0) | 75.0 (73.3, 89.7)  | 0.716                       | 0.002                       |
| ICP (mm Hg)    | 4.0 (2.0, 10.0)                                              | 3.0 (2.0, 6.0)     | 4.0 (4.0, 10.0)   | 0.163                       | 7.0 (5.8, 11.0)                                                | 7.0 (6.0, 9.0)    | 6.0 (5.0, 11.0)    | 0.728                       | < 0.001                     |
| CPP (mm Hg)    | 74.7 (69.6, 86.8)                                            | 79.3 (70.3, 92.3)  | 72.3 (67.7, 80.3) | 0.342                       | 68.7 (60.6, 82.7)                                              | 67.7 (57.0, 86.0) | 69.0 (61.7, 86.0)  | 0.650                       | < 0.001                     |
| CVP (mm Hg)    | 8.0 (5.0, 10.0)                                              | 8.0 (7.0, 10.0)    | 7.0 (4.0, 10.0)   | 0.630                       | 12.0 (10.0, 14.0)                                              | 13.0 (11.0, 15.0) | 11.0 (9.0, 13.0)   | 0.112                       | < 0.001                     |

Data are presented as median (interquartile range).

<sup>a</sup>The *p* value of inter-group comparison. <sup>b</sup>The *p* value of pre-after comparison (low positive end-expiratory pressure to high positive end-expiratory pressure) in the whole study population.

HR, heart rate; MAP, mean arterial pressure; ICP, intracranial pressure; CPP, cerebral perfusion pressure; CVP, central venous pressure

**Table E4** Changes in intracranial pressure and hemodynamic parameters from low to high positive end-expiratory pressure level (high-low)

|                | All patients        | Responders          | Non-responders    | <i>p</i> value |
|----------------|---------------------|---------------------|-------------------|----------------|
| HR (beats/min) | 1.0 (-2.0, 8.0)     | 1.0 (-1.0, 4.0)     | 1.0 (-10.0, 9.0)  | 0.870          |
| MAP (mm Hg)    | -6.8 (-11.4, -1.1)  | -9.0 (-13.3, -3.7)  | -5.7 (-9.3, 3.0)  | 0.115          |
| ICP (mm Hg)    | 2.5 (1.0, 4.0)      | 4.0 (3.0, 5.0)      | 1.0 (1.0, 2.0)    | <0.001         |
| CPP (mm Hg)    | -11.0 (-14.3, -2.6) | -13.0 (-18.3, -6.7) | -6.7 (-11.3, 1.0) | 0.011          |
| CVP (mm Hg)    | 4.0 (3.0, 5.3)      | 5.0 (4.0,5.0)       | 3.0 (1.0,6.0)     | 0.077          |

Data are presented as median (interquartile range).

HR, heart rate; MAP, mean arterial pressure; ICP, intracranial pressure; CPP, cerebral perfusion pressure; CVP, central venous pressure

**Table E5** Blood gas analysis at low and high positive end-expiratory pressure

|                                       | Low positive end-expiratory pressure (5 cm H <sub>2</sub> O) |                    |                     |                             | High positive end-expiratory pressure (15 cm H <sub>2</sub> O) |                    |                     |                             |                             |
|---------------------------------------|--------------------------------------------------------------|--------------------|---------------------|-----------------------------|----------------------------------------------------------------|--------------------|---------------------|-----------------------------|-----------------------------|
|                                       | All patients                                                 | Responders         | Non-responders      | <i>p</i> value <sup>a</sup> | All patients                                                   | Responders         | Non-responders      | <i>p</i> value <sup>a</sup> | <i>p</i> value <sup>b</sup> |
| pH                                    | 7.40 (7.36, 7.44)                                            | 7.40 (7.35, 7.43)  | 7.42 (7.37, 7.44)   | 0.481                       | 7.42 (7.38, 7.45)                                              | 7.38 (7.34, 7.44)  | 7.42 (7.39, 7.45)   | 0.228                       | 0.951                       |
| PaO <sub>2</sub> (mm Hg)              | 105.5 (78.0, 153.5)                                          | 95.0 (76.7, 130.0) | 129.0 (78.4, 168.0) | 0.242                       | 115.5 (78.4, 163.5)                                            | 98.0 (79.1, 171.0) | 125.0 (76.4, 153.0) | 0.677                       | 0.058                       |
| PaO <sub>2</sub> /FiO <sub>2</sub>    | 264 (180, 384)                                               | 274 (156, 325)     | 323 (196, 420)      | 0.144                       | 289 (185, 388)                                                 | 242 (179, 403)     | 313 (191, 383)      | 0.349                       | 0.061                       |
| PaCO <sub>2</sub> (mm Hg)             | 35.3 (32.6, 36.7)                                            | 35.4 (32.7, 38.1)  | 35.1 (30.9, 36.1)   | 0.307                       | 35.3 (33.6, 38.2)                                              | 36.4 (35.0, 40.1)  | 34.0 (31.4, 36.6)   | 0.105                       | 0.052                       |
| PETCO <sub>2</sub> (mm Hg)            | 29.5 (27.8, 31.2)                                            | 29.0 (26.0, 31.0)  | 30.0 (28.0, 32.0)   | 0.594                       | 29.0 (25.8, 30.3)                                              | 29.0 (24.0, 30.0)  | 29.0 (28.0, 31.0)   | 0.533                       | 0.003                       |
| V <sub>Dalv</sub> /V <sub>T</sub> (%) | 13.2 (8.5, 19.9)                                             | 15.1 (11.3, 29.4)  | 9.1 (7.6, 14.8)     | 0.149                       | 18.8 (11.9, 27.7)                                              | 24.4 (15.7, 30.8)  | 16.0 (8.8, 23.5)    | 0.074                       | < 0.001                     |

Data are presented as median (interquartile range).

<sup>a</sup>The *p* value of inter-group comparison. <sup>b</sup>The *p* value of pre-after comparison (low positive end-expiratory pressure to high positive end-expiratory pressure) in the whole study population.

PETCO<sub>2</sub>, end-tidal carbon dioxide partial pressure; V<sub>Dalv</sub>/V<sub>T</sub>, ratio of the alveolar dead space to the tidal volume

**Table E6** Changes in blood gas analysis from low to high positive end-expiratory pressure level (high-low)

|                                            | All patients          | Responders             | Non-responders        | <i>p</i> value |
|--------------------------------------------|-----------------------|------------------------|-----------------------|----------------|
| pH                                         | 0.001 (-0.023, 0.017) | -0.005 (-0.032, 0.008) | 0.006 (-0.010, 0.019) | 0.067          |
| PaO <sub>2</sub> (mm Hg)                   | 6.2 (-4.0, 19.6)      | 16.0 (-4.0, 22.6)      | 4.2 (-4.0, 17.0)      | 0.267          |
| PaO <sub>2</sub> /FiO <sub>2</sub> (mm Hg) | 15.4 (-10.0, 47.6)    | 30.3 (-10.0, 55.0)     | 10.5 (-10.0, 42.5)    | 0.367          |
| PaCO <sub>2</sub> (mm Hg)                  | 0.8 (-0.5, 2.5)       | 1.2 (-0.1, 3.0)        | 0.6 (-1.7, 2.0)       | 0.184          |
| PETCO <sub>2</sub> (mm Hg)                 | -1.0 (-3.0, 0)        | -1.0 (-3.0, 0)         | -1.0 (-3.0, 0)        | 0.935          |
| V <sub>Dalv</sub> /V <sub>T</sub> (%)      | 3.2 (0.8, 9.0)        | 3.6 (0.1, 11.2)        | 2.9 (0.9, 6.9)        | 0.520          |

Data are presented as median (interquartile range).

PETCO<sub>2</sub>, end-tidal carbon dioxide partial pressure; V<sub>Dalv</sub>/V<sub>T</sub>, ratio of the alveolar dead space to the tidal volume